



# **ANALYSIS OF THE CAUSES OF ALLERGIC DISEASES IN THE HUMAN BODY AND THE EFFECTS OF DRUGS USED AGAINST THEM**

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The immune system of the body plays an important role in the occurrence of allergies. It is known that this system resists most microorganisms that enter the body and cause disease, cutting off or reducing their action. The activity and structure of the immunobiological system are quite complex, and the function of protecting the body is performed mainly by the lymphatic system. It includes the thymus gland (thyroid gland), lymphatic follicles and nodes, spleen, blood, etc. Lymphocytes (T, B-lymphocytes) take an active part in the formation of immunity. It has been established that the immunobiological system resists the emergence and development of many diseases (cancer, rheumatism, etc.). At the same time, this system also causes the formation of a number of diseases. These diseases include allergic diseases.

## **SUBSTANCES THAT CAUSE ALLERGIES ARE CALLED ALLERGENS.**

They are widely distributed in nature and are divided into exo- and endoallergens. Exoallergens are substances that affect the body from the external environment (chemicals, drugs, household items, plants, etc.), and endoallergens are substances that are produced in the body itself (for example, during burns). It is known that after taking drugs, they enter the bloodstream and undergo metabolism under the action of genetically generated enzymes (oxidation, hydrolysis, conjugation, etc.). The residues of certain substances resulting from this can also act as allergens. Drugs used against allergies, depending on the mechanism of action, are divided into two groups: antihistamines and various antiallergic drugs.

## **AMIGISTAMINE DRUGS.**

Antihistamines - drugs that act against histamine and eliminate allergy symptoms are divided into 3 groups according to the mechanism of action:

- histamine blockers;

- drugs that reduce the content of histamine in the blood;
- Drugs that block the release of histamine from Ehrlich cells.

## **VARIOUS DRUGS USED AGAINST ALLERGIES.**

In the treatment of allergy sufferers, in addition to H1-histamine blockers, drugs belonging to different groups are widely used, but in general they reduce the inflammatory process. These are mainly corticosteroids and calcium preparations. Thus, the drugs used against allergic diseases are currently diverse.

## **THE SIMPLEST AND MOST EFFICIENT**

The way to treat patients with allergies is to identify the allergen and prevent it from entering the body. An allergic reaction can be caused by factors such as fungal diseases, genetic predisposition, observation of an allergy, or long-term use of the drug. It is also possible that drugs taken for a long time for chronic diseases accumulate in the body and cause various allergic conditions. For this reason, it is emphasized that in the treatment of such diseases it is necessary to take medicines with a break. If you are allergic to a drug, do not rush to treat yourself with another drug. In such situations, it is advisable to carry out the necessary treatment after cleaning the body with anti-inflammatory drugs.

When does a drug reaction occur?

When a reaction to a drug occurs, it is not a mistake to confuse it with a simple allergy.

Primary symptoms are typical for allergies.

In that:

- redness, itching in the skin area;
- allergic rhinitis;
- shortness of breath;
- symptoms such as redness of the inside of the eye and frequent tearing may be observed. At the same time, there are serious complications of drug



reactions. In particular, these include attacks of bronchial asthma, falling into a state of anaphylactic shock.

### **FIRST AID**

Before taking or administering an unfamiliar drug, it is important to take steps to avoid adverse reactions. If this is a drug in the form of a tablet, you should carefully examine its contents. In the case of an injection, a small amount should be injected into the body through a needle and it should be observed whether there is an effect. If Bodo reacts, the area of skin where the injection was given will be red and swollen. As we mentioned above, if your body doesn't like the medications you're taking and you're noticing a few signs of it, you can do the following:

- stop taking any medication;
- eat little for 2-3 days after the onset of allergy symptoms;
- do not eat foods that cause allergies for several tens of days;
- at the first sign, drink more fluids and drink boiled or non-carbonated water;
- be examined by an allergist to prevent further complications of allergies and, if necessary, receive the necessary treatment.

### **SIDE EFFECTS**

When buying a medicine, you must carefully read the instructions: it is important to pay attention to "Side effects" and for which diseases it is not recommended. Also, if you choose a drug without diagnostics, you should study its compatibility with other types.

### **LABORATORY METHODS FOR DIAGNOSING DRUG ALLERGIES**

Allergen-specific laboratory methods are the main methods for diagnosing many types of allergies, including drug allergies. General indications for the use of laboratory methods for the detection of drug allergy (LA):

- Patients with drug intolerance;
- patients with aggravated allergic anamnesis;
- patients with occupational allergies (for diagnosis and employment);
- unclear cases for diagnosis, suspicion of visceral forms of drug allergy;
- the need to exclude pseudo-allergic reactions (PAR) when administering drugs and medications to patients with a predisposition to PAR;
- the desire of patients and / or the doctor (before the introduction of the drug, surgery, etc.).

Mandatory indications for preliminary laboratory examination of patients for drug tolerance:

- shock, history of severe tokeidermia due to an unknown drug and the need for drug therapy
- for the examination of young children and adults with drug intolerance, when skin tests are non-demonstrative or negative for histamine;
- with extensive skin lesions (severe toxidermia) and the need to select tolerated drugs (antibiotics, etc.);
- against the background of taking antimediator drugs, if necessary, the introduction of potentially dangerous drugs and medicines.

Specific methods of allergy diagnostics are aimed at:

- detection of free antibodies in blood serum and secrets;
- detection of antibodies associated with leukocytes (basophils, neutrophils, platelets, etc.);
- determination of T- and B-lymphocytes sensitized to the allergen.

### **DETERMINATION OF ANTIBODIES IN THE BLOOD**

The indirect test for degranulation of basophils (Shelley) and mast cells (Schwartz) are common methods for detecting IgE class reagents. The principle of the reaction is that basophils and mast cells are able to bind the Fc fragments of the IgE antibody of the patient's blood serum with their Fc receptors. In this passive way, they are sensitized to allergens, the addition of which causes degranulation. The target cells of the reaction are rabbit blood leukocytes (pseudobasophils), rat mast cells or donor leukocytes. The indirect method of ejection of potassium ions from leukocytes is used to detect antibodies in the blood serum. The leukocytes of a healthy person are treated with the serum of a patient with an allergy, and if there were antibodies in it, then they contacted the leukocytes. The added allergen binds to the antibodies and causes a release of potassium from the leukocytes.

### **ANTIBODY BINDING ASSAYS ARE HIGHLY SENSITIVE.**

They use antibodies or allergens labeled with an isotope, fluorescein, or an enzyme. Among these methods, the most common radioallergosorbent test (RAST) and enzyme immunoassay (ELISA). Enzyme immunoassay involves the use of antibodies labeled with an enzyme rather than an isotope.

The essence of ELISA is that when the test serum is added, containing IgE antibodies to the allergen associated with the polystyrene surface of the microplate, an allergen complex is formed - IgE antibody. The amount of bound IgE, ie antibodies, is determined using enzyme-labeled anti-IgE antibodies.



To do this, anti-IgE antibodies labeled with horseradish peroxidase (or other enzyme) are added to wells washed from serum. As a result, anti-IgE antibodies specifically bind to IgE present in the atlergen-IgE antibody complex. Subsequently, reagents are added and peroxidase activity is detected by a color reaction. The ELISA method is sensitive and reproducible for the detection of antibodies of various classes in drug allergies.

It correlated in 26.9% with an intradermal test for penicilloylpolylysine, and RAST in 15% with an allergy to penicillin, and IgE antibodies were not detected in RAST in those cases in which they were found by ELISA. When testing 350 sera of patients with penicillin hypersensitivity, 105 ELISA detected antibodies of the IgG and / or IgM class, in RPHA only 49 of these 105 sera. The ELISA method, like RAST, detects only an "excess" of IgE free antibodies in the blood serum, but does not detect antibodies bound to basophils and other leukocytes. Therefore, a negative test does not guarantee the absence of "armed" IgE basophils in the patient and the development of an allergic reaction.

A positive test for specific IgE indicates the presence of an allergy.

Determination of antibodies associated with leukocytes and platelets

On the surface of all leukocytes, there are Fc receptors that bind Fc fragments of immunoglobulins-antibodies of various classes, including those with antibody specificity. Therefore, on the one hand, leukocytes with the help of these antibodies can specifically interact with allergen antigens, on the other hand, the concentration of antibodies in the blood decreases and often because of this they are not detected in the blood serum. Basophils have Fcε-receptors that bind IgE, and neutrophils have Fcγ that fix gG and may have Fcε.

Several types of reactions are based on the detection of these classes of antibodies. The results of a combination of direct and indirect potassium ion ejection reactions coincide with a well-established diagnosis in 87% of cases. Cases of discrepancy were in polyvalent allergy and in the acute period of allergy. Antibodies associated with platelets are detected in the platelet aggregation test or the release of potassium ions (see above) under the influence of the corresponding drug.

It is better to evaluate the results using an aggregometer.

Diagnosis of delayed-type allergy and lymphocyte sensitization

Currently, more and more data are accumulating on the role of T-cell recognition in LA triggering. T-cell clones have been isolated that are

sensitized to certain epitopes of small molecules such as lidocaine and β-lactams that can trigger delayed-type allergic reactions (Tx1) and/or antibody synthesis (Tx2). We believe that T-cell sensitization to allergy is present in any type of allergic reaction. In the case of sensitization of T-lymphocytes to the allergen, their proliferation and differentiation are activated and their synthesis and secretion of a number of cytokines are enhanced. B-lymphocytes carrying membrane BCRs (Ig monomers) to the allergen, apparently also participate in these reactions, releasing cytokines under the influence of such an allergen. With the help of such tests, it is possible to detect the body's sensitization to a number of aplegens (proteins, polysaccharides, peptides), as well as to simple substances, for example, to salts of a number of metals.

T-cell sensitization is detected by:

- 1) by their release of cytokines (PCCT mediators) in reactions of suppression (inhibition) of leukocyte migration, inhibition of leukocyte adherence;
- 2) by changing T-active rosette formation;
- 3) to increase the proliferation of T cells under the influence of allergens - the reaction of blast transformation with a morphological blast of blasts or to increase the inclusion of slow T I-thymidine in their DNA and in other tests, or to increase the expression of activation molecules - CD25 and others.

New opportunities in terms of assessing the stimulation of lymphocytes by causative allergens are provided by a test for enhancing the expression of IL-2 receptors on them. After the addition of an allergen, including a drug, in case of sensitization of lymphocytes to it, receptors for IL-2 are stimulated on them already after 6-18 hours.

We assessed the increase in the expression of these receptors using monoclonal antibodies to the CD25 antigen.

### **A SET OF LABORATORY METHODS THAT PROVIDE RELIABLE DIAGNOSIS OF ALLERGIES**

Anamnesis and skin tests do not always provide reliable information about the presence of LA and they cannot be used for severe skin lesions, as well as for anaphylactic shock, or the possibility of its development due to an unclear history. In young children, sometimes in older people with LA, skin tests are negative. Therefore, laboratory methods for detecting allergies for safety and the possibility of using in any period of the disease remain preferable. However, as experience shows, the use of even the most sensitive tests (RAST, ELISA) did not allow in some cases to reliably assess the tolerability of drugs. As already mentioned, IgE, IgG antibodies can bind to an allergen, to leukocytes and other cells that



have receptors for their Fc fragment. In addition, a delayed-type hypersensitivity reaction (PDHT) may develop when antibodies are not detected. In connection with the above, it is necessary to use a complex of laboratory methods for a reliable diagnosis of drug allergy. To do this, we have developed protocols for the minimum and maximum complex of laboratory methods.

The protocol of the minimum set of methods includes:

1. Determination of IgE and IgG antibodies to the drug in blood serum by ELISA and in an indirect test for the release of potassium ions.

2. Determination of total antibodies associated with the patient's leukocytes in direct reactions of the release of potassium ions, enzymes (myeloperoxidase, tryptase) and degranulation of basophils. The choice of these methods for the minimum complex is explained by the fact that reactions of the anaphylactic type depend on IgE and IgG antibodies.

A direct test for the release of potassium ions from leukocytes under the influence of the drug (see above) supplemented the ELISA in 14% of cases, although, in turn, it was negative in 12% of cases with a positive ELISA-IgE.

The parallel use of two tests provided the diagnosis of anaphylactic-type reactions in 90% of cases. However, this set of methods does not guarantee the diagnosis of all reactions of intermediate and delayed type.

The protocol of a full range of methods that provides the diagnosis of all types of hypersensitivity includes:

1. Identification of reactions of anaphylactic, IgE-dependent type:

- determination in blood serum of IgE antibodies to the drug by ELISA and / or in an indirect test for the release of potassium ions;

- determination of IgE antibodies associated with basophils (direct basophil degranulation test, direct tests for the release of potassium ions and / or myeloperoxidase)

2. Registration of immunocomplex reactions:

- IgM and IgG antibodies in blood serum (ELISA), indirect tests for the release of potassium ions, enzymes, microprecipitation;

3. Reactions of cytotoxic and intermediate (delayed) type;

- determination of IgG antibodies associated with granulocytes (in reactions of damage to granulocytes, release of potassium ions)

- detection of IgG platelet-dependent reactions (tests of platelet aggregation and degranulation under the influence of drugs)

4. Diagnosis of T-cell and delayed reactions:

- test of drug stimulation of expression of CD25 and other activation molecules;

- reaction of suppression of migration or adhesion of leukocytes, reaction of blast transformation of lymphocytes;

5. Diagnosis of pseudo-allergic reactions;

- tests of increased non-specific sensitivity of leukocytes (emission of potassium ions) to agents-inducers and an alternative pathway of complement activation;

With any positive test for the drug, it should not be prescribed to the patient, and in case of emergency, its use requires additional examination using skin tests and the introduction of trial doses. In conclusion, an allergy is a reaction of the body to foreign influences. An increase in histamine in the body leads to an increase in allergic diseases. Any product consumed in excess of the norm can subsequently cause allergies.

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